## II. RESPONSE TO OFFICE ACTION

### A. Status of the Claims

The Action indicates that claims 1-9 and 26-36 have been withdrawn from consideration, and that claims 10-25 are currently under examination. Claims 10, 13, 16, and 18-24 have been amended in the Amendment set forth herein. New claims 37-85 have been added. Claim 17 has been canceled without prejudice or disclaimer.

Support for the amendments to the original claims and the new claims can be found throughout the specification. Exemplary support can be found in paragraphs [0004], [0006]-[0010], [0014], [0017] [0018] and in the originally filed claims.

### B. Election/Restriction

The Action indicates that "Applicants' election, without traverse, of the Group II claims, claims 16-25, in the reply filed on 26 March 2004 is acknowledged" and that claims 1-15 and 26-35 are withdrawn from further consideration pursuant to 37 CFR §1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim." This is incorrect. In a response to the Restriction Requirement that is dated March 23, 2004, Applicants elected, without traverse, to prosecute claims 10-15 and 16-25, *i.e.*, the Group II claims.

### C. Claim Objections

The Action indicates that claim 10 is objected to because it depends from non-elected claims. Applicants have amended claim 10 in the Amendment filed with this response, such that claim 10 is now an independent claim. Furthermore, claim 13 has been amended such that it

now depends from elected claim 10 rather than claim 6. Therefore, the objection to claim 10 has been overcome.

## D. The Claim Rejections Under 35 U.S.C. §112, First Paragraph, are Overcome

### *1. Rejection of Claims Drawn to Fusion Proteins is Moot*

Claims 10-25 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner asserts that claims drawn to "fusion proteins" are very broad, and there is insufficient written description support since the disclosure fails to describe common attributes or characteristics that identify members of the genus of fusion proteins. Applicants respectfully traverse.

Without conceding that the claims as originally written lacked written description support in the specification, Applicants draw the Examiner's attention to amended claims 10, 13, and 16. These claims no longer recite "fusion proteins." The remaining claims at issue in this rejection depend from claims 10 or 16, and do not recite "fusion proteins." Therefore, the rejection is moot.

Based on the foregoing, it is respectfully requested that the written description of claims 10-25 under 35 U.S.C. §112, first paragraph, should be withdrawn.

### *2. Rejection of Claims Drawn to a Gene*

Claims 16-25 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement because the word "gene" is said to refer to not only a coding sequence but to "an entire genomic structure," and that the word "gene" represents "a broad genus of molecules for which the entire genomic structure of a representative number of

eukaryotic 'genes' is not known." Office Action, page 4, paragraph 3. The Examiner suggests replacing the word "gene" with terminology such as "nucleic acid sequence" in these claims. Office Action, page 4, paragraph 3.

Without conceding that the claims as originally written lacked written description support in the specification, Applicants draw the Examiner's attention to amended claim 16, which now pertains to "introducing a nucleic acid encoding a recombinant seven transmembrane G-protein associated receptor" rather than "transferring a gene." Claim 17 has been canceled without prejudice or disclaimer in the Amendment set forth herein. Therefore, any reference to the word "gene" in the claim language has been deleted, and replaced with "nucleic acid," as per the suggestion of the Examiner. Because "gene" has been replaced with "nucleic acid" in the claims at issue in this rejection, Applicants have overcome the rejection.

Therefore, Applicants respectfully request that the written description rejection of claims 16-25 under 35 U.S.C. §112, first paragraph, should be withdrawn.

### 3. There is Adequate Written Description Support in the Specification for the Amended Claims and New Claims

As set forth above, claims 10, 13, 16, and 18-24 have been amended in the Amendment set forth herein, and new claims 37-65 have been added. Applicants assert that there is sufficient written description support throughout the specification for each and every limitation of the amended claims and the new claims.

Exemplary support for "isolated nucleic acid encoding a SSTR amino acid sequence" includes paragraphs [0006]-[0009] and [0013]. Exemplary support for "wherein the encoded SSTR amino acid sequence comprises a carboxy terminal truncation" can be found in paragraph [0006] and [0065]. Exemplary support for "wherein the carboxy terminal truncation results in

alteration of internalization and/or signaling of said SSTR amino acid sequence into a cell" can be found in paragraphs [0065] and [0073]. Exemplary support for "protein tag fused to the N-terminal end or C-terminal end of said SSTR amino acid sequence can be found in paragraph [0007], [0010] and [0065]. Exemplary support for "recombinant seven transmembrane G-protein associated receptor" can be found in paragraph [0004]. Exemplary support for "subject" can be found in paragraph [0014]. Exemplary support for "detecting cellular expression of a recombinant seven transmembrane G-protein associated receptor" can be found in paragraphs [0014]-[0017] and [0063] and [0068]. Exemplary support for "wherein said recombinant seven transmembrane G-protein associated receptor is detected by contacting said cell with a ligand that binds with specificity to said recombinant seven transmembrane G-protein associated receptor" can be found in [0010], [0015], and [0016]. Exemplary support for "reporter," "Herpes simplex virus 1 thymidine kinase amino acid sequence," "dopamine receptor amino acid sequence," and "sodium/iodide symporter amino acid sequence" can be found in paragraph [0003]. Exemplary support for C-terminal truncation at amino acid 314 can be found in paragraph [0058].

Therefore, the written description requirement for the amended and new claims has been met because the specification would reasonably convey to one of ordinary skill in the art that the inventors had possession of the claimed invention.

## E. The Claim Rejections Under 35 U.S.C. §112, Second Paragraph, are Overcome

Claims 16-25 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 16 is rejected because the phrase "an expression vector according to claim 10" is unclear because claim 10 does not include an expression vector. As discussed above, claim 16 has been amended in the Amendment set forth herein. Claim 16 no longer recites "an expression vector according to claim 10." Instead, subpart (a) of claim 16 now includes the limitation of "introducing a nucleic acid encoding a recombinant seven transmembrane G-protein associated receptor into a cell of the subject." Therefore, this rejection is moot.

The Action indicates that claims 18 and 19 are unclear because of a number of plausible interpretations of these claims since there is no nexus between the limitations of these method claims and the polynucleotide of claim 10. As per the Amendment set forth herein, claim 16 has been amended so that it no longer recites "a host cell with an expression vector according to claim 10" and thus no longer depends from claim 10. Claim 18 depends from claim 16, and claim 19 depends from claim 18. In view of the Amendment set forth herein, there is no basis for lack of clarity in the claim language because there is a clear nexus between claims 16, 18, and 19. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph, should be withdrawn.

## F. The Rejections Under 35 U.S.C. §102(e) are Overcome

Claims 10-17 and 24 are rejected under 35 U.S.C. §102(e) as being anticipated by Glucksmann *et al.*. Glucksmann *et al.* is said to disclose constructs and host cells comprising a GST-receptor fusion proteins attached to a signal sequence. Glucksmann *et al.* is also said to

teach identification of fusion protein expression in a transgenic animal based on the expression of mRNA in tissues or cells of the animal. Applicants respectfully traverse the rejection.

It is a well-established principle in patent law that "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Inherent anticipation arises when "the prior art necessarily functions in accordance with, or includes, the claimed limitations." *Atlas Powder Co.*, 190 F.3d at 1347. (citing *In re King*, 801 F.2d 1324, 11326 (Fed. Cir., 1986); see also *Atlas Powder Co.,* 190 F.3d at 1347-48). Furthermore,

> "inherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

*Mehl/Biophile Int'l. Cor. V. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999) (quoting *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981).

A rejection based on 35 U.S.C. §102(e) can be overcome by persuasively arguing that the claims are patentably distinguishable from the prior art, amending the claims to patentably distinguish over the prior art, or filing an affidavit or declaration under 37 C.F.R. §1.132 showing that the reference invention is not by "another." See *MPEP* §706.02(b).

### 1. The Rejection of Claims 10-15 is Overcome

Without conceding that any of the claims at issue in this rejection were anticipated by Glucksmann *et al.*, Applicants draw the Examiner's attention to amended claim 10, which now recites "[a]n isolated nucleic acid encoding a somatostatin receptor (SSTR) amino acid sequence,

wherein the encoded SSTR amino acid sequence comprises a carboxy terminal truncation, and wherein said carboxy terminal truncation results in alteration of internalization and/or signaling of said SSTR amino acid sequence into a cell." Glucksmann *et al.* fails to anticipate claim 10 because it fails to expressly or necessarily disclose an isolated nucleic acid encoding a somatostatin receptor amino acid sequence. Glucksmann *et al.* appears to Applicants to fail to include any reference to SSTR amino acid sequences. Rather, Glucksmann *et al.* pertains to certain purportedly novel "14273 receptors," which is a type of receptor that is separate and distinct from SSTR. Furthermore, there does not appear to be any mention in Glucksmann *et al.* of any SSTR amino acid sequence comprising a carboxy terminal truncation, or any disclosure pertaining to such a truncation resulting in alteration of internalization and/or signaling of an SSTR amino acid sequence into a cell. Applicants invite the Examiner to point out any such disclosure in Glucksmann *et al.*

Furthermore, Glucksmann *et al.* fails to expressly or necessarily disclose an expression vector comprising a nucleic acid sequence encoding a somatostatin receptor amino acid sequence (claim 11), or any host cell transformed with such a vector (claim 12). In addition, Glucksmann *et al.* does not disclose a nucleic acid sequence encoding a somatostatin receptor sequence and a protein tag (claim 13), or any expression vector comprising such a nucleic acid sequence operably linked to a promoter (claim 14), or any host cell transformed with such an expression vector (claim 15). None of these limitations are inherently present in Glucksmann *et al.* since, as noted above, Glucksmann *et al.* pertains to an entirely different receptor than SSTR, and there is no mention whatsoever of SSTR in Glucksmann *et al.*

In view of the above, Glucksmann *et al.* fails to anticipate claims 10-15 because it fails to expressly or inherently disclose each and every element of the claimed invention. Applicants therefore respectfully request that the rejection under 35 U.S.C. §102(e) should be withdrawn.

**2. The Rejection of Claim 16, 17, and 24 is Overcome**

Without conceding that any of the claims at issue in this rejection were anticipated by Glucksmann *et al.*, Applicants draw the Examiner's attention to amended claim 16, which now pertains to "[a] method of detecting cellular expression of a recombinant seven transmembrane G-protein associated receptor in a subject comprising: (a) introducing a nucleic acid encoding a recombinant seven transmembrane G-protein associated receptor into a cell of the subject, and (b) detecting cellular expression of a recombinant seven transmembrane G-protein associated receptor based upon the chemical, physical or biological properties of said recombinant seven transmembrane G-protein associated receptor." As set forth above, claim 17 has been canceled in the Amendment set forth herein. Amended claim 24 pertains to "[t]he method of claim 39, wherein the expression of said recombinant seven transmembrane G-protein associated receptor is detected by enzymatic activity of said protein tag. New claim 39 pertains to "[t]he method of claim 38, wherein said protein tag has enzymatic activity." New claim 38 pertains to "[t]he method of claim 22, wherein said recombinant seven transmembrane G-protein associated receptor further comprises a protein tag fused to the N-terminal end or C-terminal end of said recombinant seven transmembrane G-protein associated receptor. Claim 22 in turn depends from claim 16.

Glucksmann *et al.* fails to anticipate claims 16 and dependent claim 24 because it fails to expressly or inherently disclose "detecting cellular expression of a recombinant seven transmembrane G-protein associated receptor based upon the chemical, physical, or biological

properties of said recombinant seven transmembrane G-protein associated receptor." As discussed above, the disclosure in Glucksman *et al.* pertains to certain purportedly novel 14273 receptors that are said to belong to the superfamily of G-protein-coupled receptors (GPCRs). Paragraph [0299] in Glucksmann *et al.*, cited by the Examiner in the Action, indicates that "[a] transgenic founder animal can be identified based upon the presence of the transgene in its genome and/or expression of transgenic mRNA in tissues or cells of the animal." The procedure set forth in Glucksmann *et al.* is for the purpose of detecting transgenic founder animals. The method of detection by measurement of mRNA set forth in Glucksmann *et al.* is ***not*** a method of measurement of cellular expression of a recombinant seven transmembrane G-protein associated receptor that is ***based upon the chemical, physical, or biological properties of the recombinant seven transmembrane G-protein associated receptor***. Measurement of mRNA is not a form of measurement that depends upon any chemical, physical, or biological properties of the receptor protein that is expressed at the cellular level. Nor are such methods inherently disclosed in Glucksmann *et al.* since measurement of mRNA does not necessarily require measurement of any particular chemical, physical, or biological property of the actual receptor protein that is expressed in the cell.

Dependent claim 24 includes the additional limitation of wherein expression of the recombinant seven transmembrane G-protein associated receptor is detected by enzymatic activity of a protein tag. No such method of measuring expression of a recombinant seven transmembrane G-protein associated receptor in a cell of a subject is disclosed in Glucksmann *et al.*

For the reasons set forth above, there is no anticipation by Glucksmann *et al.* under 35 U.S.C. §102(e). Therefore, Applicants respectfully request that the rejection under 35 U.S.C. §102(e) should be withdrawn.

## G. The Rejections Under 35 U.S.C. §103(a) are Overcome

### 1. Glucksmann *et al.* Further in View of Eisenhut *et al.*

The Action indicates that claims 10-18, 20, 21 and 24 are rejected under 35 U.S.C. §103(a) as being unpatentable over Glucksmann *et al.* as applied to claims 10-17 and 24 (as set forth under the 35 U.S.C. §102(e) rejection), and further in view of Eisenhut *et al.* (U.S. 2001/0029035). The teachings of Glucksman *et al.* alleged by the Examiner are set forth above. Eisenhut *et al.* is said to teach the use of a PNA peptide conjugate, which includes the use of octreotide labeled with $^{125}I$ to determine the distribution of the conjugate in organs, and that octreotides are somatostatin analogs that bind the somatostatin receptor. According to the Examiner, it would have been obvious to one of ordinary skill in the art to use radioactive octreotides to measure expression of fusion proteins that comprise somatostatin receptors. Therefore, the invention as a whole is said to be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Applicants respectfully traverse.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (3) there must be a reasonable expectation of success.

*Manual of Patent Examining Procedure* § 2142. See also *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed Cir. 1991). It is important to note that all three elements must be shown to establish a *prima facie* case of obviousness. Thus, if one element is missing, a *prima facie* case of obviousness does not exist.

Furthermore, the Examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the Examiner does not produce a *prima facie* case, the Applicant is under no obligation to submit evidence of nonobviousness. See *Manual of Patent Examining Procedure* (MPEP) §2142.

**a. The Rejection of Claims 10-15 is Overcome**

There is no *prima facie* case of obviousness because the Examiner has not shown how the combination of prior art references teaches or suggests each of the claim limitations. It appears to Applicants that Glucksmann *et al.* fails to render obvious claim 10 because it fails to teach or suggest an isolated nucleic acid encoding any truncated somatostatin receptor amino acid sequence. In fact, Glucksmann *et al.* does not appear to Applicants to make any reference to SSTR amino acid sequences. Rather, Glucksmann *et al.* pertains to certain purportedly novel "14273 receptors," which is a type of receptor that is separate and distinct from SSTR. Furthermore, does not appear to be any mention in Glucksmann *et al.* of any SSTR amino acid sequence comprising a carboxy terminal truncation, or any disclosure pertaining to such a truncation resulting in interference of internalization of an SSTR amino acid sequence into a cell. If the Examiner knows of such teachings or suggestions, Applicants request that he provide these on the record.

Regarding the dependent claims 11-15, the Action set forth by the Examiner provides no indication pertaining to how Glucksmann *et al.* teaches or suggests an expression vector comprising a nucleic acid sequence encoding a somatostatin receptor amino acid sequence (claim 11), or any host cell transformed with such a vector (claim 12). In addition, Glucksmann *et al.* does not appear to teach or suggest a nucleic acid sequence encoding a somatostatin receptor sequence and a protein tag (claim 13), or any expression vector comprising such a nucleic acid sequence operably linked to a promoter (claim 14), or any host cell transformed with such an expression vector (claim 15). None of these limitations appear to be suggested in Glucksmann *et al.* since, as noted above, Glucksmann *et al.* pertains to an entirely different receptor than SSTR, and there is no mention whatsoever of SSTR in Glucksmann *et al.* Again, if the Examiner knows of any teaching or suggestion of these claim limitations, Applicants request that these be set forth in the record.

Furthermore, the Examiner has not provided any indication in the Action that the missing limitations are provided by Eisenhut *et al.* It appears to Applicants that Eisenhut *et al.* pertains to certain oligonucleotide conjugates, and not isolated nucleic acids. Importantly, Eisenhut et al. discusses the ligand, and not the receptor. In vitro binding assays were used to demonstrate biodistribution of the ligand. No mention is made of recombinant receptors. The nucleotides that are part of the oligonucleotide set forth in Eisenhut *et al.* comprise a sequence at least part of whose sequence is complementary to an intracellular nucleic acid sequence. The oligonucleotides envisioned are too small to encode a protein. There is no indication whatsoever that the nucleotide component of the conjugates set forth in Eisenhut *et al.* encode somatostatin receptor sequences, or somatostatin receptor sequences that are truncated.

Furthermore, as to dependent claims, Eisenhut *et al.* has not been shown to teach or suggest any expression vector, such as an expression vector comprising a nucleic acid that encodes a somatostatin receptor amino acid sequence comprising a carboxy terminal truncation (claim 11). Nor does Eisenhut *et al.* teach host cells transformed with such a vector (claim 12). Eisenhut *et al.* also fails to teach or suggest an isolated nucleic acid that encodes any truncated SSTR amino acid sequence wherein the nucleic acid further encodes a protein tag (claim 13). Nor does it teach expression vectors comprising such a nucleic acid sequence (claim 14), or host cells transformed with such a vector (claim 15). Applicants request that the Examiner provide on the record any such teaching or suggestion pertaining to each of these claim limitations, if such teaching or suggestion is present.

Therefore, because the Examiner has failed to establish that each of the claim limitations are taught or suggested by the combination of references set forth, there is no *prima facie* case of obviousness under 35 U.S.C. §103(a). Applicants therefore respectfully request withdrawal of the rejection.

**b. The Rejection of Claim 16, 17, and 24 is Overcome**

The Examiner has not established a *prima facie* case of obviousness because he has not shown on the record how the cited combination of prior art references teaches or suggests each of the claim limitations.

The Examiner has not shown how Glucksmann *et al.* teaches or suggests "detecting cellular expression of a recombinant seven transmembrane G-protein associated receptor based upon the chemical, physical, or biological properties of said recombinant seven transmembrane G-protein associated receptor." As discussed above, the disclosure in Glucksman *et al.* pertains to certain purportedly novel 14273 receptors that are said to belong to the superfamily of G-

protein-coupled receptors (GPCRs). Paragraph [0299] in Glucksmann *et al.*, cited by the Examiner in the Action, indicates that "[a] transgenic founder animal can be identified based upon the presence of the transgene in its genome and/or expression of transgenic mRNA in tissues or cells of the animal." The procedure set forth in Glucksmann *et al.* is for the purpose of detecting transgenic founder animals. The method of detection by measurement of mRNA set forth in Glucksmann *et al.* is ***not*** a measurement of cellular expression of the recombinant protein that is ***based upon the chemical, physical, or biological properties of the recombinant seven transmembrane G-protein associated receptor***. Nor are such methods suggested in Glucksmann *et al.* since measurement of mRNA is not associated with any particular chemical, physical, or biological property of the receptor protein that is expressed at the cellular level. Applicants request that if the Examiner knows of any such teaching or suggestion of this claim limitation, that he provide in on the record.

Claim 24 includes the additional limitation of wherein expression of the recombinant seven transmembrane G-protein associated receptor is detected by enzymatic activity of a protein tag. Once again, the Examiner has not indicated in the Action how such method of measuring expression of a recombinant seven transmembrane G-protein associated receptor in a cell of a subject is taught or suggested in Glucksmann *et al.*

Furthermore, the Examiner has not shown how the missing claim limitations are taught or suggested by Eisenhut *et al.* Eisenhut *et al.* appears to pertains to an oligonucleotide conjugate comprising an oligonucleotide at least part of whose sequence is complementary to an intracellular nucleic acid sequence, and a somatostatin analog, and medicaments containing this oligonucleotide conjugate. The oligonucleotides set forth in Eisenhut *et al.* do not appear to include nucleic acids encoding a recombinant seven transmembrane G-protein associated

receptor. Nor is there any mention of ***detecting cellular expression*** or *in vivo* imaging of a recombinant seven transmembrane G-protein associated receptor. Eisenhut *et al.*, paragraph [0012] appears to discloses octreotide as one example of a somatostatin analog. Paragraph [0015] – [0016] of Eisenhut *et al.*, cited by the Examiner, provides no indication that the oligonucleotide conjugates containing octreotide were used to detect cellular expression of a recombinant seven transmembrane G-protein associated receptor. Applicants invite the Examiner to identify any such teaching or suggestion in Eisenhut *et al.*

Therefore, the Examiner has not met his burden of showing how the cited combination of references teaches or suggests all limitations of the claimed invention. As a result, there is no *prima facie* case of obviousness under 35 U.S.C. §103(a). Applicants therefore respectfully request withdrawal of the rejection.

**2. Glucksmann *et al.* Further in View of Koller *et al.***

Claims 10-16 and 22-24 are rejected under 35 U.S.C. §103(a) as being unpatentable over Glucksmann *et al.* as applied to claims 10-17 and 24 above, and further in view of Koller *et al.* The teachings of Glucksmann *et al.* alleged by the Examiner are set forth above. Koller *et al.* is said to teach the use of a hemagluttinin A sequence fused to a receptor as a means of identifying the expressed receptors. The expressed protein is said to be identified by the binding of hemagluttinin A to the commercially available antibody, 12CA5. The Examiner indicates that it would have been obvious to one of ordinary skill in the art to use antibodies that bind the antibodies that bind hemagluttinin A to measure expression of the fusion proteins of the invention that comprise hemagluttinin A. The Examiner also indicates that one of ordinary skill in the art would have been motivated to use antibodies because they allow for one of skill in the art to identify expressed fusion proteins that comprise particular sequences and structural

characteristics to which the antibodies bind. The Examiner indicates that Koller *et al.* exemplifies that binding assays are well known in the art and well within the purview of the ordinary skilled artisan. Therefore, the invention as a whole is said to be *prima facie* obvious. Applicants respectfully traverse.

**a. The Rejection of Claims 10-15 is Overcome**

As set forth above, the Examiner has not met his burden of demonstrating a *prima facie* case of obviousness because he has not shown how the combination of prior art references set forth teaches or suggests each of the claim limitations. As set forth above, the discussion of which is herein specifically incorporated into this section, the Examiner has not met his burden of showing how Glucksmann *et al.* teaches or suggests an isolated nucleic acid encoding a somatostatin receptor amino acid sequence, wherein the encoded somatostatin receptor amino acid sequence comprises a carboxy terminal trunction and wherein said carboxy terminal truncation results in alteration of internalization and/or signaling of said SSTR amino acid sequence into a cell. Applicants invite the Examiner to point out any teaching or suggestion in Glucksmann *et al.* pertaining to nucleic acids encoding truncated SSTR amino acid sequences.

As set forth above, the Examiner has also not met his burden of showing how Glucksmann *et al.* teaches or suggests an expression vector comprising a nucleic acid sequence encoding a somatostatin receptor amino acid sequence (claim 11), or any host cell transformed with such a vector (claim 12). In addition, the Examiner has not shown how Glucksmann *et al.* teaches or suggests a nucleic acid sequence encoding a somatostatin receptor sequence and a protein tag (claim 13), or any expression vector comprising such a nucleic acid sequence operably linked to a promoter (claim 14), or any host cell transformed with such an expression vector (claim 15).

Furthermore, the Examiner has not shown how these limitations are taught or suggested by Koller *et al.* Koller *et al.* appears to pertain to certain methods for the production of cell lines expressing high levels of 7-transmembrane receptors by N-terminal tagging these proteins with the hemagglutinin sequence. The Examiner has not shown how Koller *et al.* teaches or suggests an isolated nucleic acid sequence encoding a SSTR amino acid sequence, wherein the encoded SSTR amino acid sequence comprises a carboxy terminal truncation, wherein said carboxy terminal truncation results in alteration of internalization and/or imaging of said SSTR amino acid sequence into a cell. The generic expression vectors for 12CA5-tagged seven transmembrane receptors disclosed in Koller *et al.* do not appear to Applicants to be truncated at the carboxy terminal (see page 54 of Koller *et al.*). To truncate the SSTR receptor in such a fashion would likely result in loss of function, and would negate the purpose of the study, which appears to be to generate cell lines stably expressing high levels of a desired receptor for both binding and functional assays (see page 54 of Koller *et al.*).

Nor has the Examiner set forth how Koller *et al.* teaches or suggests an expression vector comprising a nucleic acid that encodes a somatostatin receptor amino acid sequence comprising a carboxy terminal truncation wherein the carboxy terminal truncation results in alteration of internalization and/or signaling of the SSTR amino acid sequence into the cell. In addition, the Examiner has not cited any teaching or suggestion in Koller *et al.* pertaining to host cells transformed with such a vector, or an isolated nucleic acid that encodes any SSTR amino acid that comprises a carboxy terminal truncation wherein the nucleic acid further encodes a protein tag, or expression vectors comprising such a nucleic acid sequence, or host cells transformed with such a vector.

Therefore, in view of the above, the Examiner has not met his burden of establishing a *prima facie* case of obviousness under 35 U.S.C. §103(a). Applicants therefore respectfully request withdrawal of the rejection.

**b. The Rejection of Claims 16 and 22-25 is Overcome**

The Examiner has not met his burden of demonstrating a *prima facie* case of obviousness because he has not shown how the combination of prior art references set forth teaches or suggests each of the claim limitations. As set forth above, the discussion of which is specifically incorporated into this section, the Examiner has not shown how Glucksmann *et al.* teaches or suggests detecting cellular expression of a recombinant seven transmembrane G-protein associated receptor based upon the chemical, physical, or biological properties of said recombinant seven transmembrane G-protein associated receptor in a subject.

Furthermore, the Examiner has not shown how this missing limitation is taught or suggested by Koller *et al.* It appears to Applicants that Koller *et al.* pertains to certain methods for the production of cell lines expressing high levels of functional 7-transmembrane receptors. The Examiner has not met his burden of demonstrating a teaching or suggestion in Koller *et al.* pertaining to the introduction of nucleic acids encoding recombinant seven transmembrane G-protein associated receptors into a ***subject***. Rather, the purpose of Koller *et al.* appears to be to "rapidly produce mammalian ***cell lines*** stably expressing a high level of a desired receptor" in vitro that can be "especially useful when using new methods of high-throughput screening." Koller *et al.*, page 52 (emphasis added). Thus, no *in vivo* methods are disclosed in Koller *et al.* Applicants invite the Examiner to set forth any such teaching or suggestion in the record.

Therefore, the prior art references do not teach or suggest all of the claim limitations. As a result, there is no *prima facie* case of obviousness under 35 U.S.C. §103(a). Applicants therefore respectfully request withdrawal of the rejection.

### 3. Glucksman *et al.* Further in View of Ausubel *et al.*

Claims 10-16 and 22-25 are rejected under 35 U.S.C. §103(a) as being unpatentable over Glucksmann *et al.* as applied to claims 10-16 and 24 above, and further in view of Ausebel *et al.* The teachings of Glucksmann *et al.* alleged in the Action are as set forth above. Ausubel *et al.* is said to teach common enzymatic reporters using CAT. According to the Examiner, it would have been obvious to one of ordinary skill in the art to use enzyme fusion proteins in order to identify expression of fusion protein constructs based on detection of enzymatic activity. It is also asserted that one of ordinary skill in the art would have been motivated to use CAT because it is one of many common reporter genes known in the art. The Action further notes that one of ordinary skill in the art would reasonably expect the successful use of enzyme fusion proteins using CAT as the enzyme because the use of reporters is germane to the art of molecular biology. Therefore, the invention is said to be *prima facie* obvious. Applicants respectfully traverse.

#### a. The Rejections of Claims 10-15 is Overcome

The Examiner has failed to establish a *prima facie* case of obviousness because he has not met his burden of showing how the combination of prior art references teach or suggest each of the claim limitations. As set forth above, the discussion of which is herein specifically incorporated into this section, the Examiner has not met his burden of showing how Glucksmann *et al.* teaches or suggests an isolated nucleic acid encoding a somatostatin receptor amino acid sequence, wherein the encoded somatostatin receptor amino acid sequence comprises a carboxy

terminal trunction and wherein said carboxy terminal truncation results in alteration of internalization and/or signaling of said SSTR amino acid sequence into a cell. Applicants invite the Examiner to point out any teaching or suggestion in Glucksmann *et al.* pertaining to nucleic acids encoding truncated SSTR amino acid sequences.

As set forth above, the Examiner has also not met his burden of showing how Glucksmann *et al.* teaches or suggests an expression vector comprising a nucleic acid sequence encoding a somatostatin receptor amino acid sequence (claim 11), or any host cell transformed with such a vector (claim 12). In addition, the Examiner has not shown how Glucksmann *et al.* teaches or suggests a nucleic acid sequence encoding a somatostatin receptor sequence and a protein tag (claim 13), or any expression vector comprising such a nucleic acid sequence operably linked to a promoter (claim 14), or any host cell transformed with such an expression vector (claim 15).

Furthermore, the Examiner has not shown how Ausubel *et al.* teaches or suggests these missing limitations. Ausubel *et al.* appears to Applicants to be a short report pertaining to certain genetic reporter systems, one of which is CAT. Ausubel *et al.* does not appear to Applicants to include any information pertaining to recombinant seven transmembrane G-protein associated receptors, such as SSTR, or truncated receptors. Applicants invite the Examiner to point out any such teaching or suggestion.

The Examiner has not identified how Ausubel *et al.* teaches or suggests an expression vector comprising a nucleic acid that encodes a somatostatin receptor amino acid sequence comprising a carboxy terminal truncation, or a host cells transformed with such a vector. The Examiner has also not identified any teaching or suggestion in Ausubel *et al.* pertaining to an isolated nucleic acid that encodes any SSTR amino acid that comprises a carboxy terminal

truncation wherein the nucleic acid further encodes a protein tag, or an expression vectors comprising such a nucleic acid sequence, or host cells transformed with such a vector.

Therefore, the Examiner has not met his burden of showing how the prior art references cited in this rejection teach or suggest all of the claim limitations. As a result, there is no *prima facie* case of obviousness under 35 U.S.C. §103(a). Applicants therefore respectfully request withdrawal of the rejection.

**b. The Rejection of Claims 16 and 22-25 is Overcome**

The Examiner has not met his burden of demonstrating a *prima facie* case of obviousness because he has not shown how the combination of prior art references set forth teaches or suggests each of the claim limitations. As set forth above, the discussion of which is specifically incorporated into this section, the Examiner has not shown how Glucksmann *et al.* teaches or suggests detecting cellular expression of a recombinant seven transmembrane G-protein associated receptor based upon the chemical, physical, or biological properties of said recombinant seven transmembrane G-protein associated receptor in a subject.

Nor does Glucksmann et al. teach a method of detection by contacting the cell with an antibody, antibody fragment, or small molecule that binds with specificity to the recombinant seven transmembrane G-protein associated receptor, or a method of detection involving an antibody binding with specificity to a protein tag, or a method of detection involving measurement of enzymatic activity of chloramphenical acetyl transferase.

Furthermore, the Examiner has not met his burden of showing how Ausubel *et al.* teaches or suggests this missing limitations. Applicants do not identify any teaching or suggestion in Ausubel *et al.* pertaining to recombinant seven transmembrane G-protein associated receptors, such as SSTR. Applicants invite the Examiner to identify on the record any such teaching or

suggestion. Nor has the Examiner identified any teaching or suggestion pertaining to detecting in a subject *in vivo* cellular expression of a recombinant seven transmembrane G-protein associated receptor based upon the chemical, physical or biological properties of said recombinant seven transmembrane G-protein associated receptor or any other methods of detecting cellular expression of a recombinant seven transmembrane G-protein associated receptor. The disclosure in Ausubel *et al.* does not appear to Applicants to provide any guidance to one of ordinary skill in the art to provide the limitations that are not taught or suggested by Glucksmann *et al.* Applicants invite the Examiner to identify how Ausubel *et al.* in combination with Glucksmann *et al.* teaches each limitation of the claimed invention.

Therefore, the Examiner has not met his burden of showing how the prior art references teach or suggest all of the claim limitations. As a result, there is no *prima facie* case of obviousness under 35 U.S.C. §103(a). Applicants therefore respectfully request withdrawal of the rejection.

## III. PETITION FOR EXTENSION OF TIME

Pursuant to 37 C.F.R. § 1.136(a), Applicant petitions for an extension of time of three months to and including December 18, 2004 in which to respond to the Office Action dated June 18, 2004. Pursuant to 37 C.F.R. § 1.17, a check is enclosed, which is the process fee for a three-month extension of time. If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included herein, the Commissioner is authorized to deduct or credit said fees from or to Fulbright & Jaworski Deposit Account No. 50-1212/UTSC:753US.

The Examiner is invited to contact the undersigned attorney at (512) 536-5639 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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Date: December 15, 2004